Diuretics in Heart Failure

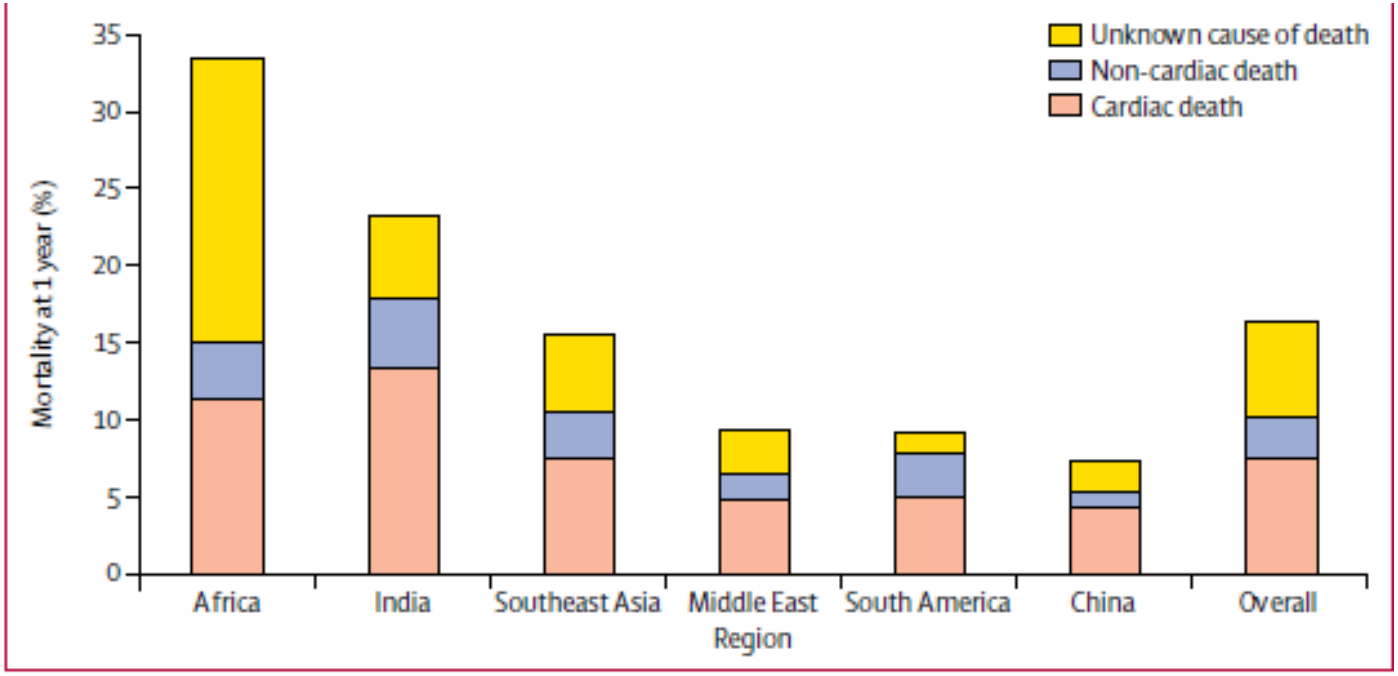
Heart Failure

Heart Failure is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/ or elevated intracardiac pressures at rest or during stress.

2016 ESC Guidelines. Ponikowski P et al. Eur J Heart Fail. 2016 Aug;18(8):891-975.

Heart Failure Burden

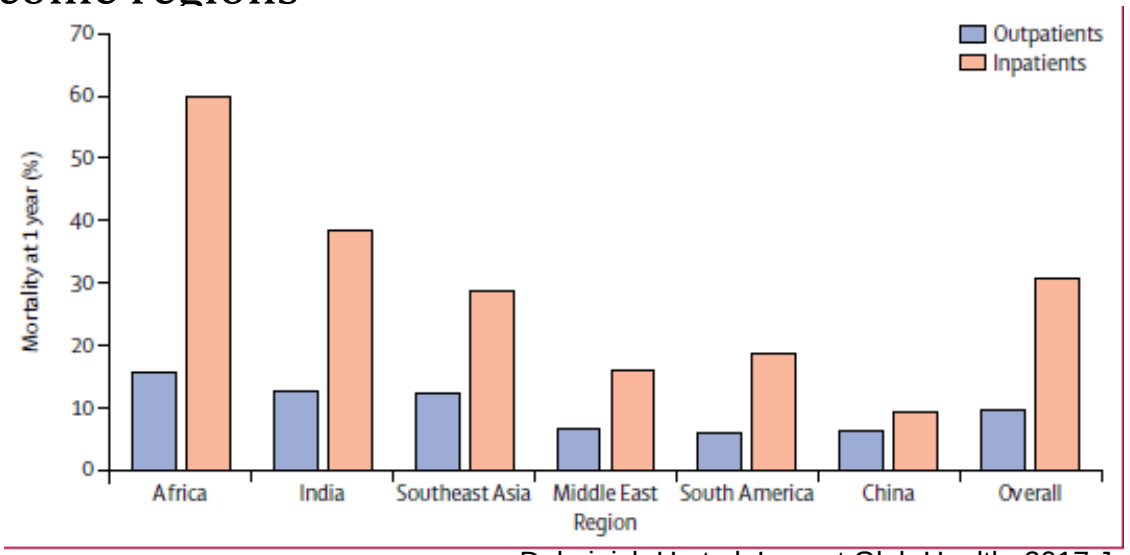
- Heart failure is an important global health problem, affecting about 26 million people worldwide
- Indians have one of the highest rates of mortality after diagnosis of heart failure, greater than that of people in several developing countries in the world



Dokainish H et al. Lancet Glob Health. 2017 Jul;5(7):e665-e672

Heart Failure Burden

- In INTER-CHF, patients in Africa, India, and southeast Asia were approx. 10 years younger than patients in South America and China
- Of the 5,823 heart failure patients observed in India, Africa, Southeast Asia, China, South America, and West Asia, two-thirds were clinic outpatients.
- Indian patients were at approximately three times the risk of death within one year compared with heart failure patients in relatively higher income regions



Dokainish H et al. Lancet Glob Health. 2017 Jul;5(7):e665-e672

Clinical: Symptoms of HF

- **Left Heart Failure**:
  - Dyspnea on exertion
  - Dyspnea at rest
  - Orthpnea
  - Paroxysmal nocturnal dyspnea (PND)
  - Fatigue, inability to exercise

- **Right Heart Failure:**
  - Swelling of feet, hands
  - Abdominal distention/fullness
  - Right upper quadrant pain
  - Early satiety
  - Weight loss (cardiac cachexia)

ACC/AHA Guidelines 2013

Clinical: Signs of HF

- **Left Heart Failure**:
  - Rales
  - Pleural effusions
  - CM: Displaced apical impulse
  - Tachycardia, LVS3, murmur of MR
  - Narrow pulse pressure

- **Right Heart Failure:**
  - Edema of lower extremities
  - Elevated JVP/+ HJR
  - RVS3, murmur of TR
  - Hepatomegaly, RUQ tenderness
  - Ascites
  - Pleural effusions

Stages of Heart Failure

Asymptomatic

A At high risk for HF but without structural heart disease or symptoms of HF (e.g., patients with HTN or CAD)

B Structural heart disease but without symptoms of HF

C Structural heart disease with prior or current symptoms of HF

D Refractory/advanced HF requiring specialized interventions

Symptomatic

NYHA Class

Class I Asymptomatic: No limitation of physical activity. Ordinary activity does not cause sxs.

II Symptomatic with moderate exertion. Ordinary physical activity causes SOB, fatigue

III Symptomatic with minimal exertion. Less than usual activity causes sxs

IV Symptomatic at rest. Unable to carry on any activity without discomfort.

ACC/AHA Guidelines 2013

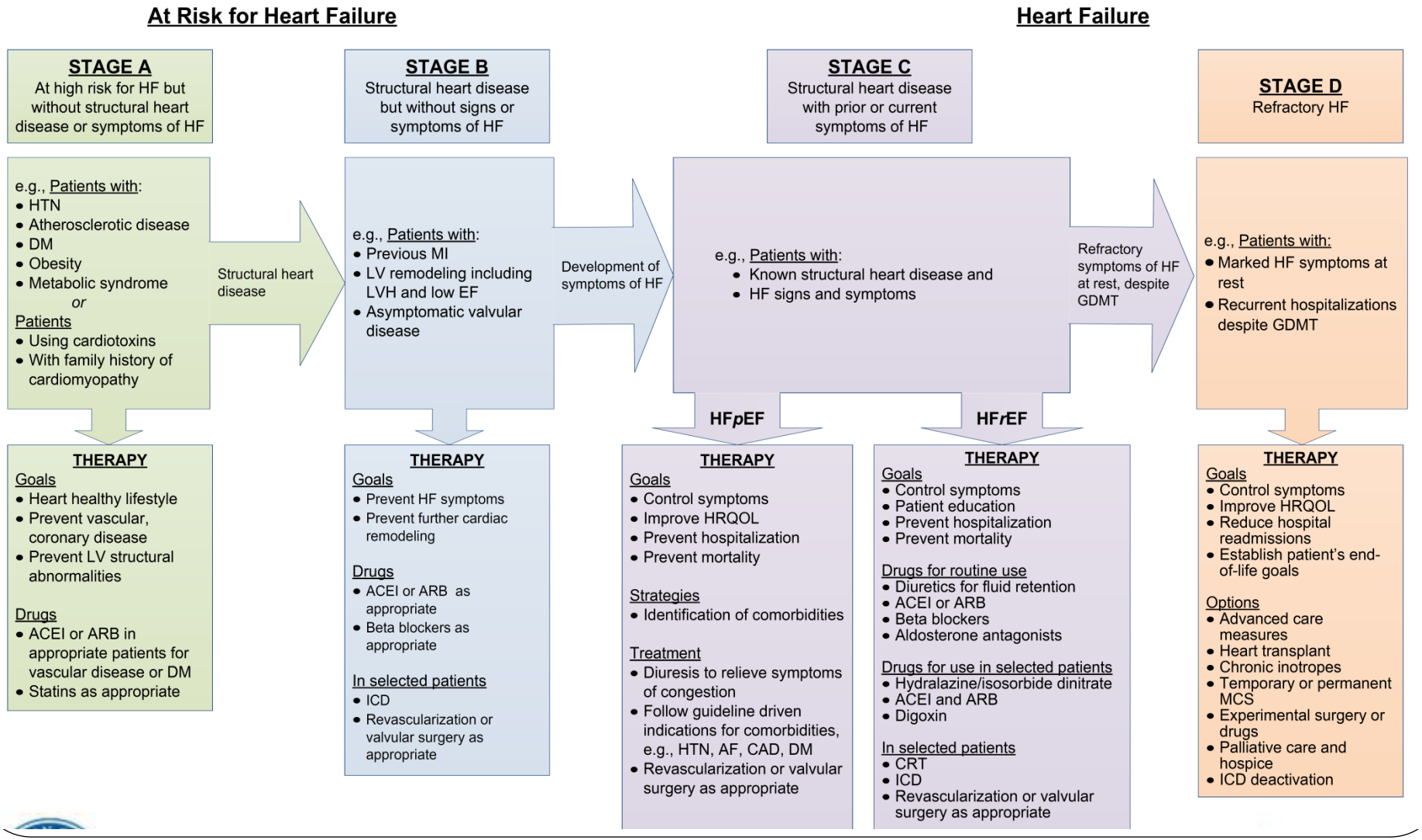
NYHA Class and Mortality

NYHA Class	1-Yr Mortality
Class I Asymptomatic: No limitation of physical activity. Ordinary activity does not cause sxs.	5-10%
II Symptomatic with moderate exertion. Ordinary physical activity causes SOB, fatigue	5-10%
III Symptomatic with minimal exertion. Less than usual activity causes sxs	10-25%
IV Symptomatic at rest. Unable to carry on any activity without discomfort.	25-60%

ACC/AHA Guidelines 2013

Management of Patients with Heart Failure

Stages, Phenotypes and Treatment of HF



Initial Workup of Stage C HF

- After detailed history; Initial laboratory evaluation:
  - CBC, urinalysis, CMP (including calcium and magnesium), fasting lipid profile, TSH, iron panel
- Serial monitoring, when indicated, should include serum electrolytes and renal function.

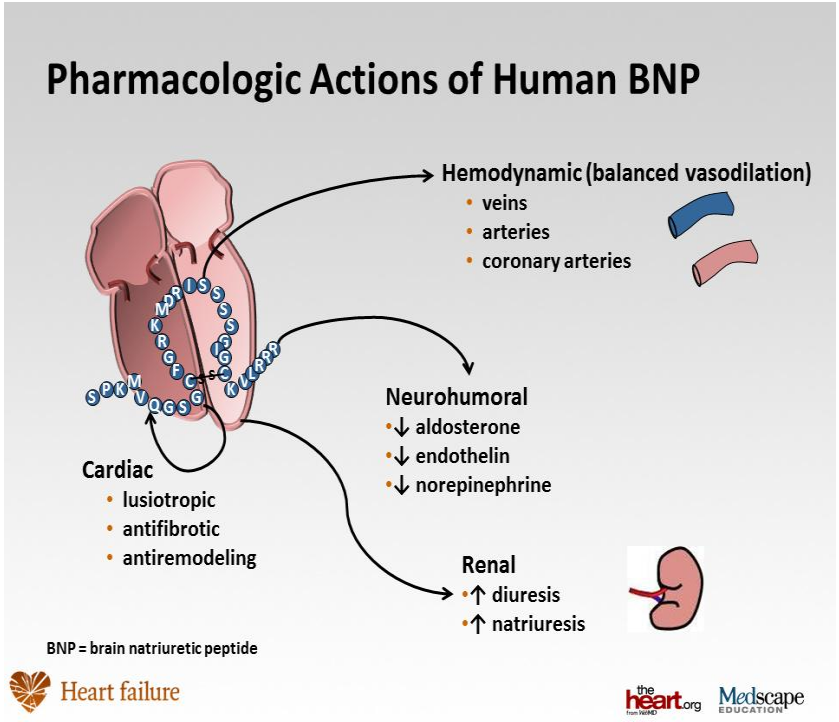
- A 12-lead ECG should be performed initially on all patients presenting with HF.

- Chest X-ray is all patients with new onset HF.

- Echocardiogram in all patients with new dx of HF (MUGA in some)
- Repeat echo usually for a significant change in clinical status or for consideration of changes after therapy or to evaluate for device therapy.

- Noninvasive stress imaging or cardiac cath is reasonable in HF and suspected CAD

BNP (NT-proBNP) in HF



- BNP or B-type natriuretic peptide is produced mostly by cardiac ventricles in response to stress/strain/stretch on the myocardium

- BNP has beneficial effects in heart failure: promotes vasodilation, diuresis and natriuresis

- Levels increased in patients with HF; levels correlate with wedge pressures and prognosis

- BNP < 100 pg/ml usually will r/o significant HF in <u>acute</u> dyspnea

BNP (NT-proBNP) in HF (2)

- Patients discharged with BNP > 400-500 pg/ml at discharge are at a higher risk for HF readmissions and mortality

- However, patients with low LVEF can have normal levels if diuresed well (20-25% chronic HF)

- Levels ↑ with age, especially in older women, and with renal dysfunction
- ↑ in HFrEF & HFpEF (overall higher in HFrEF)
- ↓ ↓ in obesity
- Elevated BNP also seen with RV dysfunction, PE

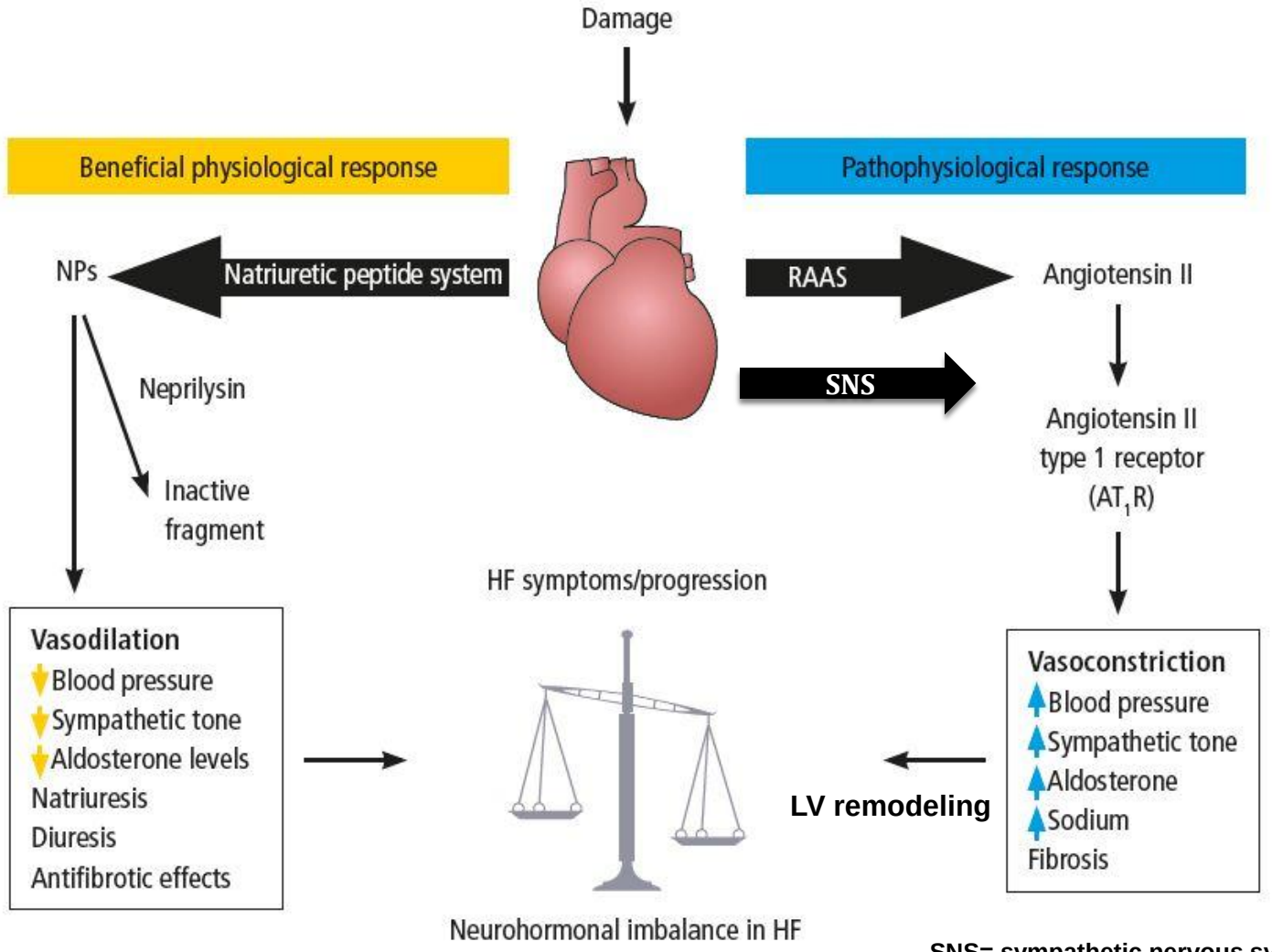
- Although prognostic- no definitive data to recommend titrating diuretics or meds to BNP levels- outside of structured HF programs.

Stage C (HFrEF & HFpEF)

- Non-pharmacologic interventions
  - Education to facilitate self care
  - Regular physical activity; cardiac rehabilitation
  - Sodium restriction
  - Treat comorbidities: **Hypertension**, diabetes, CAD, sleep apnea, anemia
  - Influenza and pneumococcal immunization
  - Decrease/stop alcohol, smoking, other drug abuse
  - *Close outpatient follow-up*

- Avoid certain drug classes:
  - NSAIDs
  - Ca channel blockers except amlodipine (in HFrEF)
  - Antiarrhythmics except amiodarone, dofetalide
  - Thiazolidinediones (TZDs)

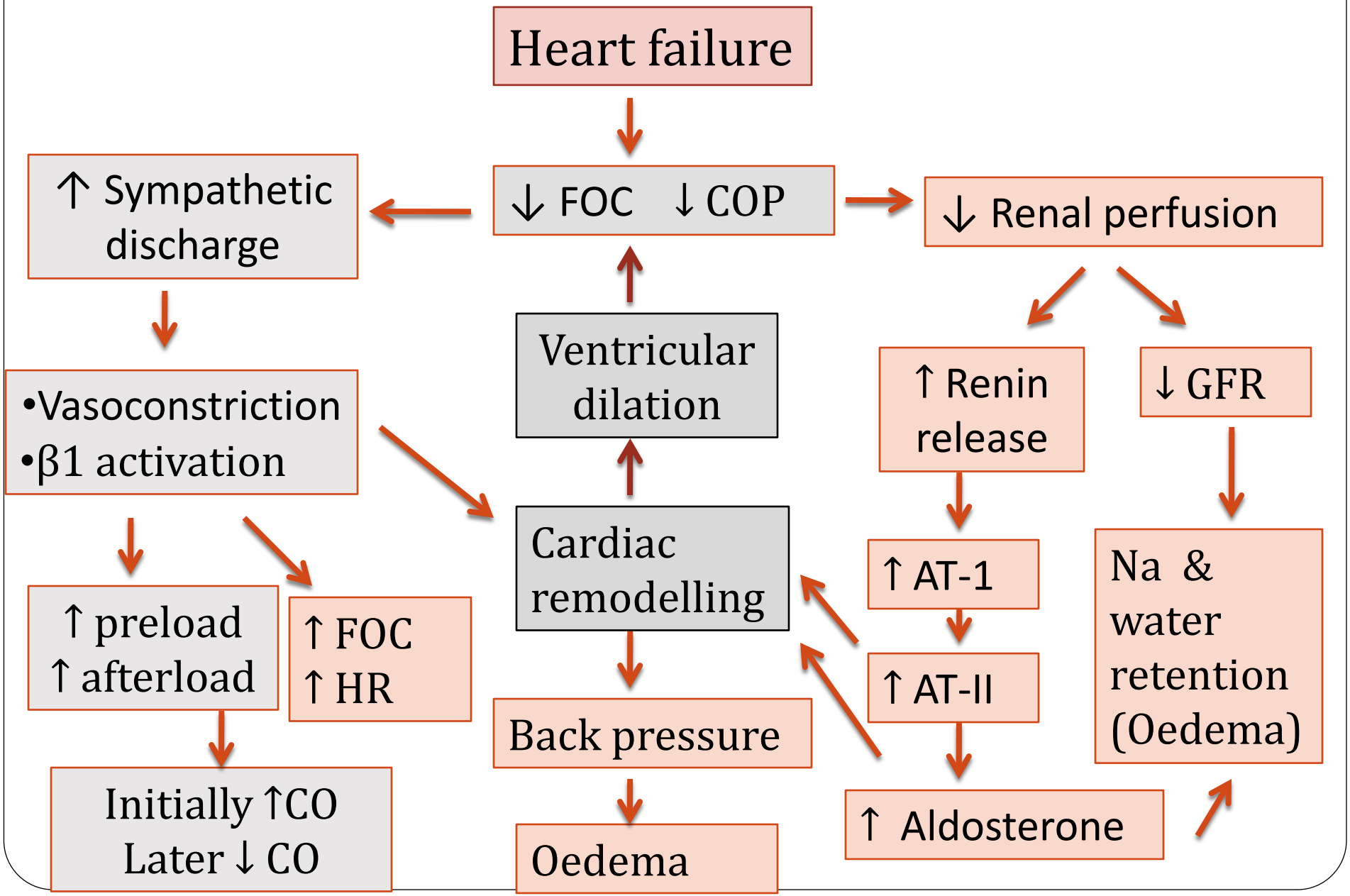
Pathophysiology of HFrEF & Therapeutic Targets

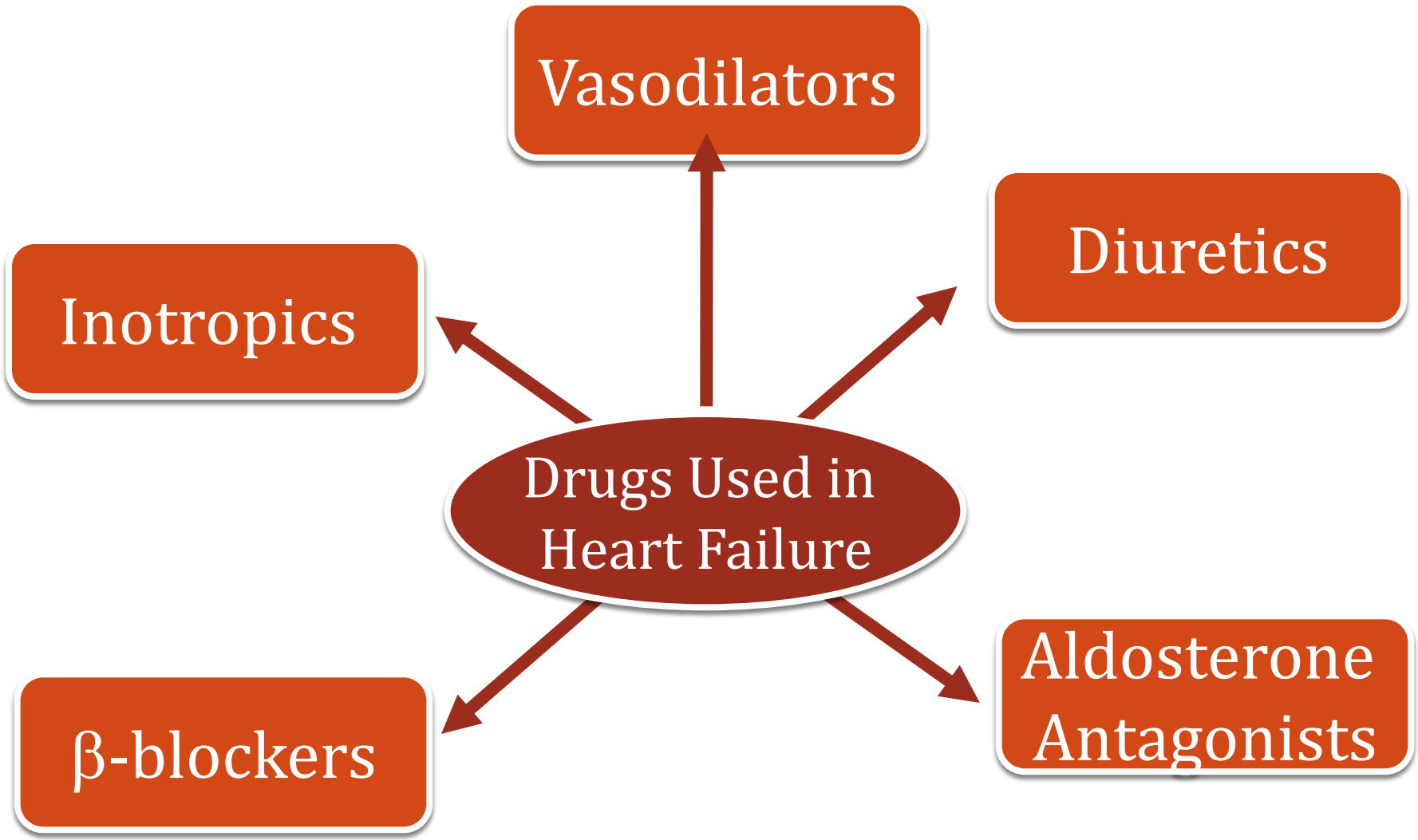


SNS= sympathetic nervous system
RAAS= Renin angiotensin aldosterone system

Adapted from Langenickel TH, Dole WP. Drug Discovery Today

Compensatory responses during heart failure




Vasodilators
Diuretics
Inotropics
Drugs Used in Heart Failure
β-blockers
Aldosterone Antagonists

Inotropic drugs

- Cardiac glycosides:
  - Digoxin, digitoxin
- Sympathomimetic amines:
  - Dopamine , dobutamine
- Phosphodiesterase inhibitors:
  - Amrinone , milrinone

Vasodilators

- Arteriolar:
  - Hydralazine , minoxidil, nicorandil
- Venodilators:
  - Nitrates
- Arteriolar and venodilators:
  - ACE inhibitors, ARBs

Diuretics

- Loop diuretics:
  - furosemide, torsemide
- Thiazide diuretics:
  - Hydrochlorthiazide
- K+ Sparing diuretics:
  - Spironolactone , Amiloride

Beta Blockers

- Metoprolol,
- Bisoprolol,
- Carvedilol

Heart Failure Treatments: Medication Types

Type	What it does
•ACE inhibitor (angiotensin-converting enzyme)	•Expands blood vessels which lowers blood pressure, neurohormonal blockade
•ARB (angiotensin receptor blockers)	•Similar to ACE inhibitor—lowers blood pressure
•Beta-blocker	•Reduces the action of stress hormones and slows the heart rate
•Digoxin	•Slows the heart rate and improves the heart's pumping function (EF)
•Diuretic	•Filters sodium and excess fluid from the blood to reduce the heart's workload
•Aldosterone blockade	•Blocks neurohormal activation and controls volume

ACE inhibitors

- **Angiotensin-converting enzyme inhibitors (ACE inhibitors) relieve symptoms and improve prognosis** and can be effective in patients with heart failure.

- **Treatment with an ACE inhibitor alone** can be considered in people with NYHA grades I-II who do not have symptoms or signs of fluid overload. Diuretics should be added if fluid overload is present.

- **Cough** is common in heart failure but is also caused by an ACE inhibitor in a small percentage of people. Cough is not a reason to stop an ACE inhibitor unless it is troublesome.

Davies MK et al. BMJ. 2000 Feb 12; 320(7232): 428–431.

https://www.uptodate.com/contents/use-of-angiotensin-converting-enzyme-inhibitors-in-heart-failure-with-reduced-ejection-fraction

B-Blockers

- **Beta-blockers are recommended for all people with heart failure (NYHA grades I-IV) whose failure is stable,** on standard treatment, unless there is a contraindication.
- **Beta-blockers in combination with other treatments,** such as ACE inhibitors, diuretics and digoxin, improve survival by more than 30% compared to standard treatment alone in people with stable heart failure.
- **Bisoprolol, carvedilol, and modified-release metoprolol have been shown to be beneficial.**

Friedrich EB, et l. Heart. 2007 May; 93(5): 626–631.

Diuretics

- **Diuretics give rapid symptom relief** and should be started early in symptomatic people with signs of fluid overload. Their long-term effects on mortality rates and other endpoints when given alone are not known (excluding spironolactone). An ACE inhibitor should always be added to diuretic therapy, unless contraindicated, as this improves prognosis.
- **Loop diuretics are usually preferred to thiazide diuretics.** Thiazides may be as effective as loop diuretics in treating oedema in people with mild failure who have preserved renal function.
- **The combination of a thiazide with a loop diuretic** gives a synergistic effect and may be useful in people with severe, persistent symptoms. Close monitoring of electrolytes is required and such treatment should usually be specialist initiated.

Remme WJ et al. Eur Heart J. 2001 Sep;22(17):1527-60.

Spironolactone

- **Spironolactone,** should be considered for people with moderate to severe heart failure (NYHA grades III-IV) who are already on an ACE inhibitor and a loop diuretic
- **The Randomised Aldactone Evaluation Study (RALES)** compared treatment with low-dose spironolactone (25 mg daily) added to standard care with other diuretics, ACE inhibitors and digoxin against standard care alone, in people with moderate to severe heart failure (NYHA III-IV).
- Mortality was reduced by 30%, the risk of hospitalization for worsening heart failure was reduced by 35%, and there was a significant improvement in symptoms. Over 2 years, one death was avoided for every 9 people treated with spironolactone in addition to standard therapy.
- **Careful monitoring for hyperkalaemia and hypovolaemia is required.**

Remme WJ et al. Eur Heart J. 2001 Sep;22(17):1527-60.

Use of diuretics in patients with heart failure

Diuretics in Heart Failure

- Evaluation and optimization of volume status is an essential component of treatment in patients with heart failure (HF).

- Removal of excess extracellular fluid with diuretics to treat peripheral and/or pulmonary edema is one of the mainstays of volume management.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Diuretics in Heart Failure

- HF remains the most common cause of hospitalisation in patients over the age of 65 and the main symptoms are vascular congestion.

- Fluid overload is a major pathophysiological mechanism underlying both acute decompensation in HF and the progression of the syndrome.

- Although there has been a lot of controversy on the possible negative effects of diuretic therapy, due to the reduced intra-arterial volume with neuro-endocrine hyperactivation, no definite causal relationship has been established between diuretic therapy, its dosage and cardiovascular mortality.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Diuretics in Heart Failure

- Three main classes of diuretics (loop diuretics, thiazide diuretics with metolazone and potassium-sparing diuretics).
- Loop diuretics are most commonly used, because they have the most potent natriuretic action.
- Conversely, despite having a weak diuretic effect, potassium sparing diuretics have been shown to be significantly efficacious in improving the long-term prognosis in symptomatic HF patients.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Diuretics in Heart Failure

- The primary role of thiazide-like diuretics in CHF is to attempt to overcome diuretic resistance.

- Thus performing a sequential nephron blockade when administered in association with loop diuretics.

Loop Diuretics

Drug	Site of Action	Duration of Action	Common Starting Dosage	Maximum Dosage	Common Side Effects
Loop diuretics	Inhibition of Na-K-Cl co-transporter in the thick ascending loop of Henle				Hypokalaemia, hypomagnesaemia, hyperuricaemia, hypocalcaemia, hyponatraemia, otoxicity
Furosemide		7 h	20 to 40 mg once or twice	600 mg	
Bumetanide		4 to 6 h	0.5 to 1.0 mg once or twice	10 mg	
Torasemide		12 to 16 h	10 to 20 mg once	200 mg	
Ethacrynic acid		6 h	25–50 mg once or twice	200 mg	

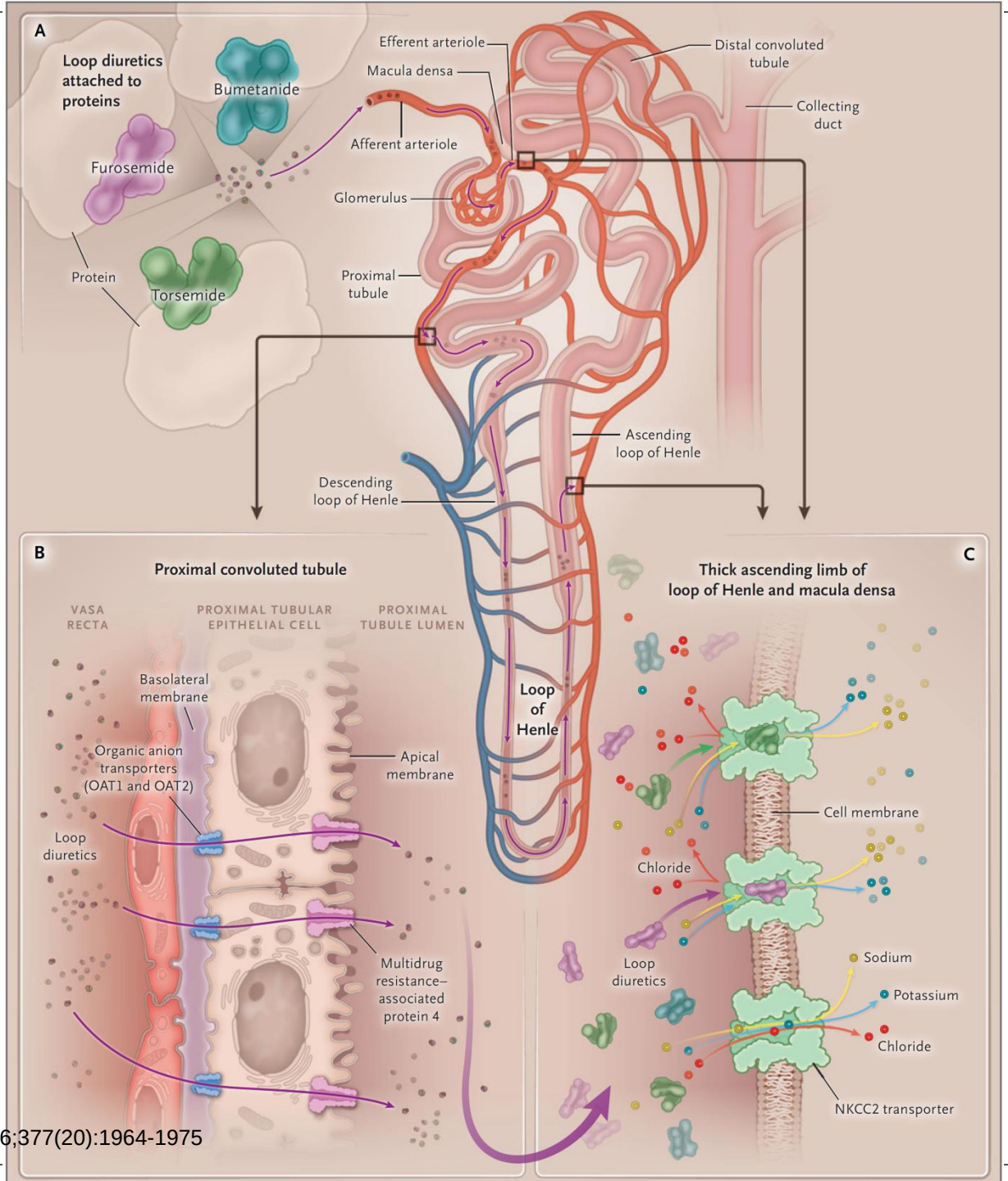
Thiazide like Diuretics

Drug	Site of Action	Duration of Action	Common Starting Dosage	Maximum Dosage	Common Side Effects
Thiazide-like diuretics	Inhibition of Na-Cl transporter at distal nephron				Hypokalaemia, hypomagnesaemia, hypercalcaemia, hyponatraemia, hyperuricaemia
Chlorothiazide		6 to 12 h	250 to 500 mg	Once or twice	1,000 mg
Chlorthalidone		24 to 72 h	12.5 to 25 mg once	100 mg	
Indapamide		36 h	2.5 mg once	20 mg	

Potassium Sparing Drugs

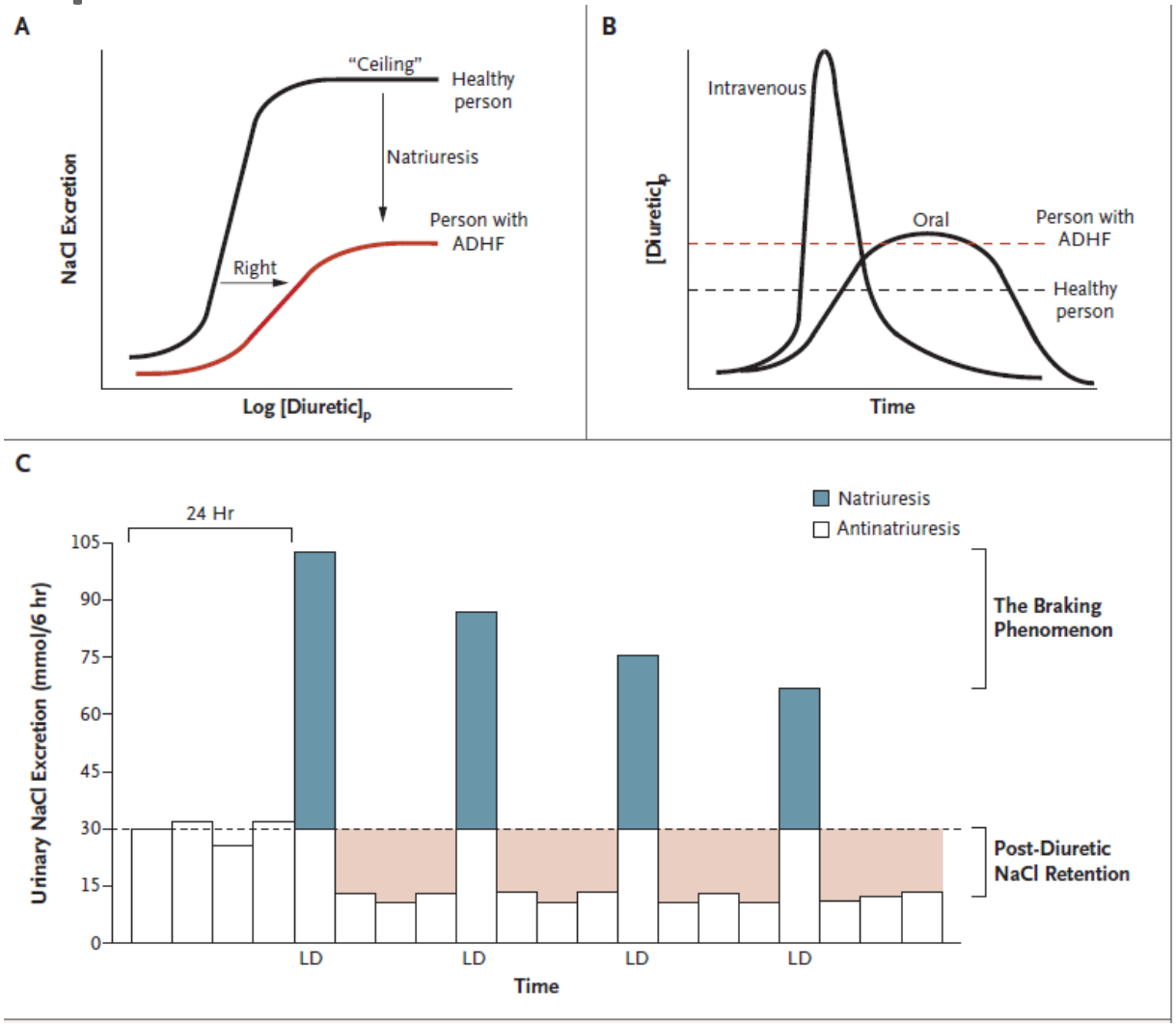
Drug	Site of Action	Duration of Action	Common Starting Dosage	Maximum Dosage	Common Side Effects
Potassium-sparing diuretics	Inhibition of mineralcarticoid receptor or its effectors at distal nephron				Hyperkalaemia
Amiloride		24 h	5 mg once	20 mg	
Triamterene		7 to 9 h	50 to 75 mg twice	200 mg	
Spironolactone		1 to 3 h	12.5 to 25.0 mg once	50 mg	Gynecomastia

Mechanisms of Loop Diuretic Action and Resistance.



Ellison DH et al. N Engl J Med. 2017 Nov 16;377(20):1964-1975

Pharmacokinetic and Pharmacodynamic Properties of Loop Diuretics.



Ellison DH et al. N Engl J Med. 2017 Nov 16;377(20):1964-1975

Causes of Diuretic Resistance

- Inadequate dose of diuretic
- Nonadherence
  - Not taking drug
  - High sodium intake
- Pharmacokinetic factors
  - Slow absorption of diuretic because of gut edema
  - Impaired secretion of diuretic into the tubule lumen
    - Chronic kidney disease
    - Aging
    - Drugs
      - Nonsteroidal antiinflammatory drugs*
      - Probenecid
- Hypoproteinemia
- Hypotension
- Nephrotic syndrome
- Antinatriuretic drugs
  - Nonsteroidal antiinflammatory drugs*
  - Antihypertensive agents
- Low renal blood flow
- Nephron remodeling
- Neurohormonal activation

* These drugs inhibit the efficacy of loop diuretics through several mechanisms.

Ellison DH et al. N Engl J Med. 2017 Nov 16;377(20):1964-1975

Treatment of Diuretic Resistance

- Diuretic resistance is defined as the failure of diuretics to achieve decongestion, which is manifest by a low urine sodium concentration, despite the use of maximal recommended doses.
- Continuous infusion of diuretic therapy is frequently used in such patients.
- A post hoc analysis has suggested that a stepped-care pharmacologic approach may be superior to standard "decongestive therapy,"

Ellison DH et al. N Engl J Med. 2017 Nov 16;377(20):1964-1975

Stepped-Care Pharmacologic Approach

Studies suggested that a stepped-care pharmacologic approach, focused on aggressive diuretic therapy and is adjusted to produce a urine volume of 3 to 5 liters per day may be superior to standard "decongestive therapy," consisting of standard high-dose loop diuretics, in patients with the cardiorenal syndrome.

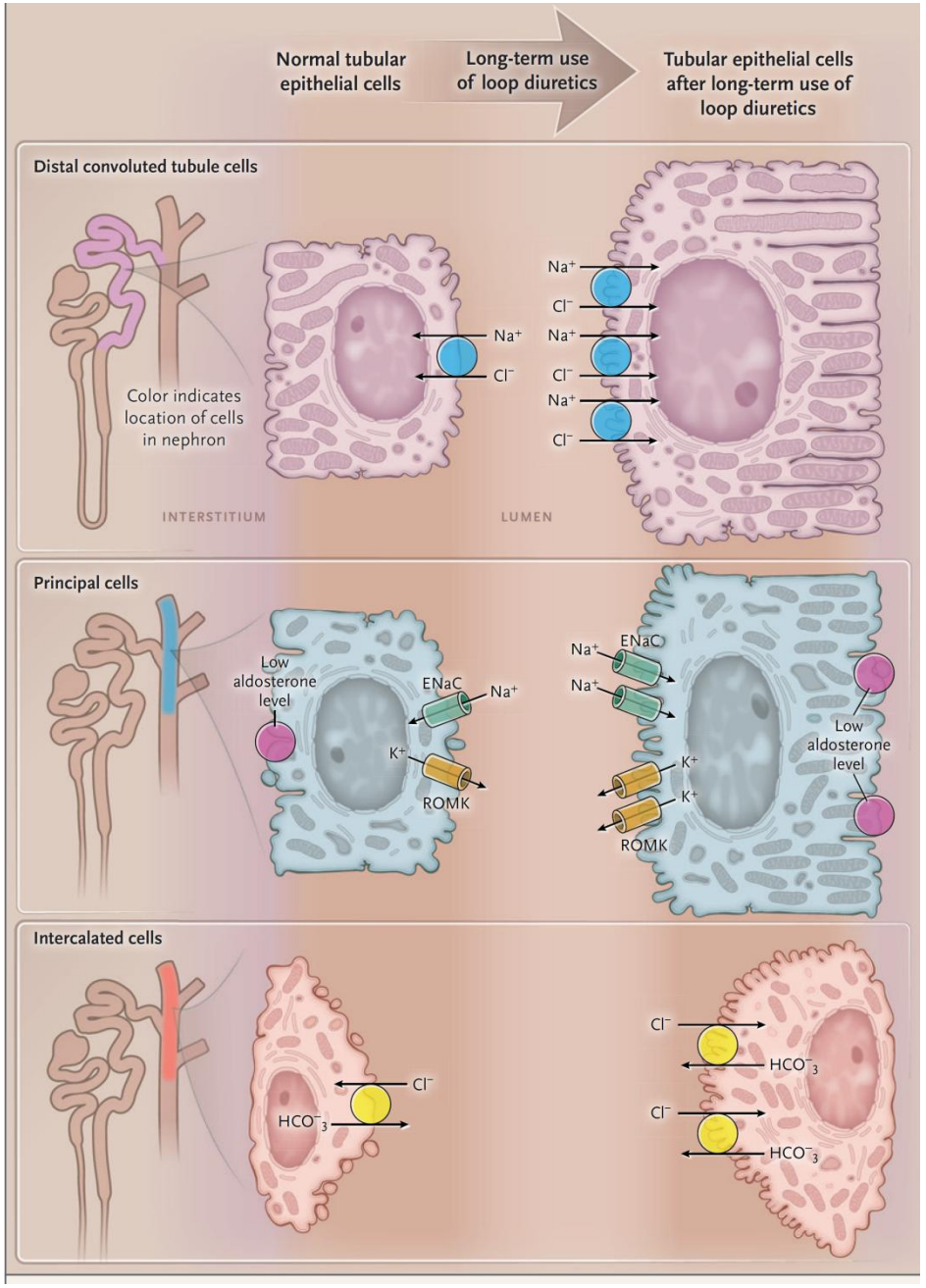
Level	Furosemide			Metolazone†
	Previous Oral Dose‡	Bolus	Infusion Rate	Oral Dose
1	≤80 mg	40 mg	5 mg/hr	NA
2	81–160 mg	80 mg	10 mg/hr	5 mg daily
3	161–240 mg	80 mg	20 mg/hr	5 mg twice daily
4	>240 mg	80 mg	30 mg/hr	5 mg twice daily

* The goal of treatment is a daily urine volume of 3 to 5 liters until clinical euvolemia is reached. The initial approach may involve the intravenous administration (in two doses) of 2.5 times the patient's previous oral daily dose of furosemide or alternatively the infusion approach described above. The diuretic level can be increased daily to achieve urinary output between 3 and 5 liters per day by moving to the next step if the urinary output remains less than 3 liters. NA denotes not applicable.

† Hydrochlorothiazide (at a dose of 50 mg twice daily) or chlorthalidone (at a dose of 50 mg daily) may be substituted for metolazone. Adapted from Grodin et al.[36] and Bart et al.[37] The full algorithm includes additional considerations for vasodilator, inotropic, or mechanical therapy in patients who do not have a response within 48 hours.

‡ A dose of 40 mg of furosemide is considered to be equivalent to 1 mg of bumetanide or 20 mg of torsemide.

Nephron Remodeling as a Mechanism of Diuretic Resistance.



Diuretics in Heart Failure

- Diuretics are the cornerstone of treatment of volume overload in patients with heart failure (HF).
- However, few clinical trials have studied the impact of diuretic therapy on clinical outcomes.
- A meta-analysis of diuretic treatment in chronic HF demonstrated a beneficial effect on clinical outcomes, although only small trials were available.

Felker GM et al. N Engl J Med. 2011;364(9):797.
Felker GM et al. Circ Heart Fail. 2009 Jan;2(1):56-62.

Diuretics in heart failure: Cochrane Review

- The review includes 14 trials (525 participants), 7 were placebo-controlled, and 7 compared diuretics against other agents such as ACE inhibitors or digoxin.
- Mortality was lower for participants treated with diuretics than for placebo, odds ratio (OR) for death 0.24, 95% confidence interval (CI) 0.07 to 0.83; P = 0.02. Admission for worsening heart failure was reduced in those taking diuretics in two trials (169 participants), OR 0.07 (95% CI 0.01 to 0.52; P = 0.01).
- In four trials comparing diuretics to active control (91 participants), diuretics improved exercise capacity in participants with CHF, difference in means WMD 0.72 , 95% CI 0.40 to 1.04; P < 0.0001.
- The available data from several small trials show that in patients with chronic heart failure, conventional diuretics appear to reduce the risk of death and worsening heart failure compared to placebo. Compared to active control, diuretics appear to improve exercise capacity.

Faris RF et al. Cochrane Database Syst Rev. 2012 Feb 15;(2):CD003838.

Diuretics in Heart Failure

- Three trials with a total of 202 patients with chronic HF found a reduction in mortality with diuretic use compared with placebo (odds ratio [OR] 0.24, 95% CI 0.07 to 0.83).

- Admission for worsening HF was reduced by diuretics compared with placebo in two trials with a total of 169 patients (OR 0.07, 95% CI 0.01 to 0.52).

- **These results are consistent with data from observational studies as well as diuretic trials demonstrating rapid improvement in dyspnea in patients treated largely with diuretic therapy.**

Felker GM et al. N Engl J Med. 2011;364(9):797.
Felker GM et al. Circ Heart Fail. 2009 Jan;2(1):56-62.

Diuretic Strategies in Patients with Acute Decompensated Heart Failure

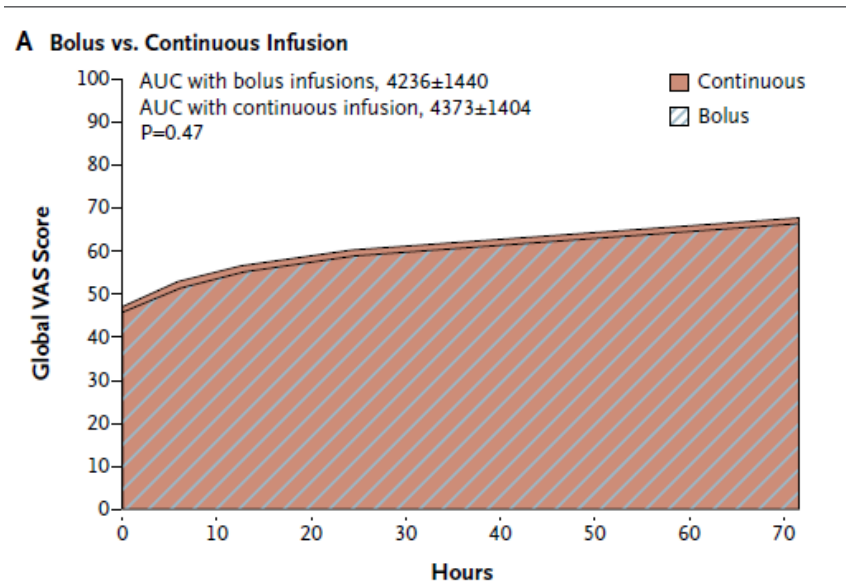
Diuretic Optimization Strategies Evaluation (DOSE) trial

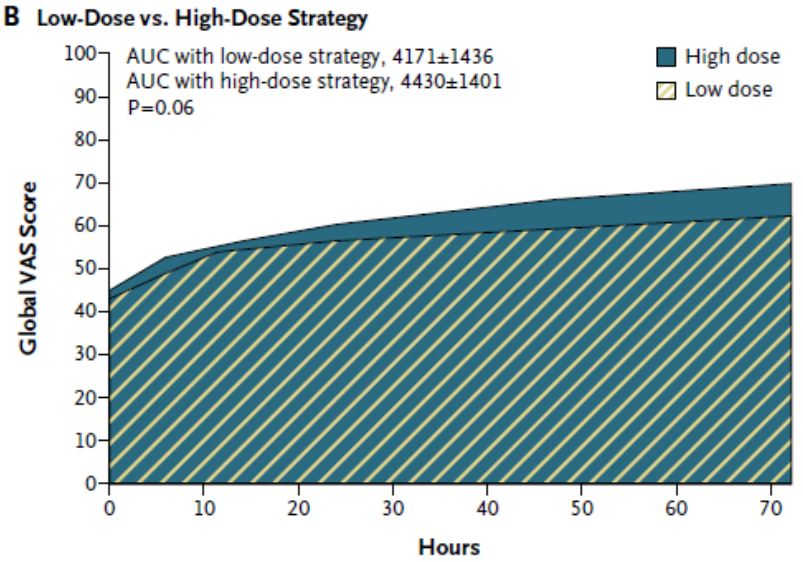
- Loop diuretics are an essential component of therapy for patients with acute decompensated heart failure, but there are few prospective data to guide their use.

- In a prospective, double-blind, randomized trial, we assigned 308 patients with acute decompensated heart failure to receive furosemide administered intravenously by means of either a bolus every 12 hours or continuous infusion and at either a low dose (equivalent to the patient's previous oral dose) or a high dose (2.5 times the previous oral dose).

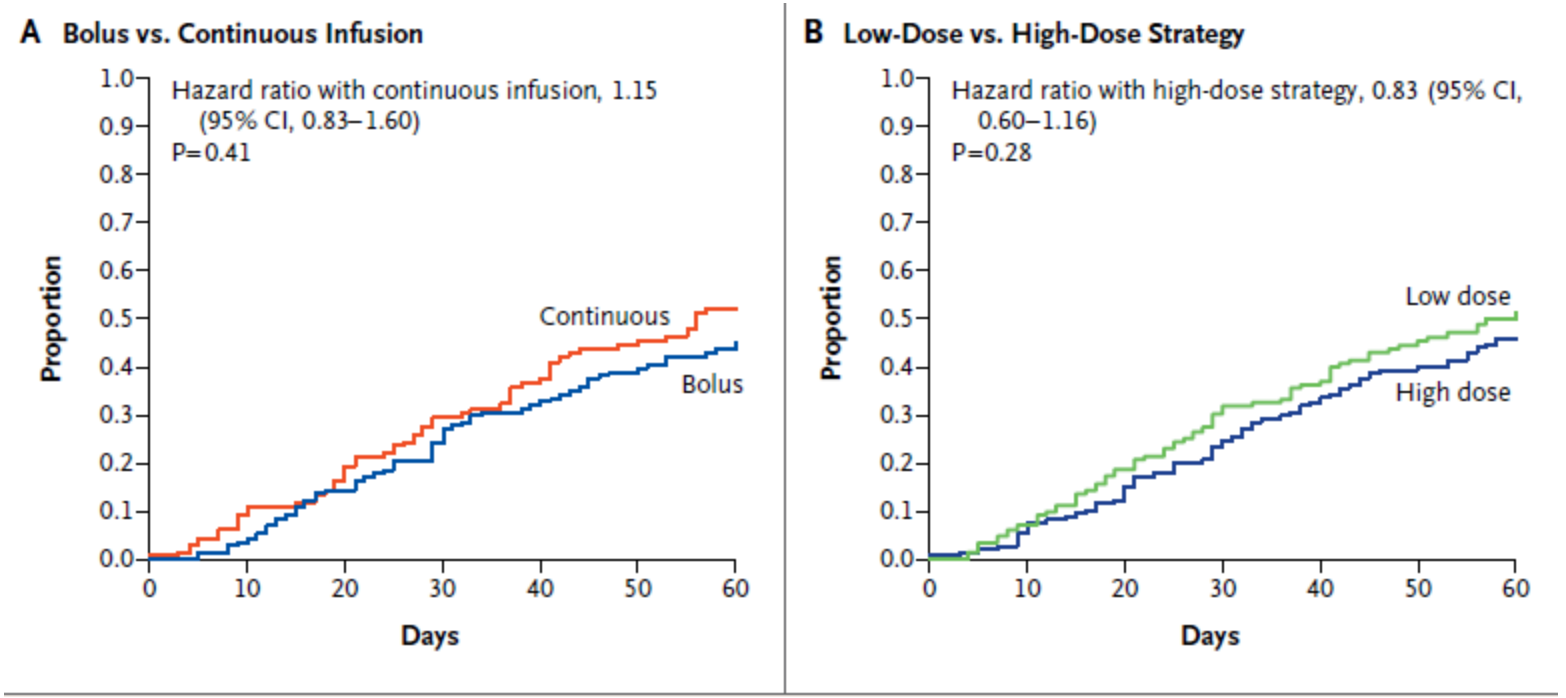
Results

Patients' Global Assessment of Symptoms during the 72-Hour Study-Treatment Period.





Results



Kaplan–Meier Curves for the Clinical Composite End Point of Death, Rehospitalization, or Emergency Department Visit.

Among patients with acute decompensated heart failure and moderate-to-high baseline diuretic requirements, there were no significant differences in the patients' global assessment of symptoms or in changes from baseline renal function with either bolus as compared with continuous infusion of intravenous furosemide or with a low-dose strategy as compared with a high dose strategy.

Felker GM et al. N Engl J Med 2011;364:797-805

CARRESS-HF study

- In a post-hoc analysis of DOSE-AHF and the Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF).
- Plasma renin activity (PRA) and serum aldosterone levels were measured to explore the relationship between RAAS activation and decongestion strategy with clinical outcomes .
- Patients who received a continuous infusion of furosemide had higher PRA levels.
- However, there was no significant difference in these biomarkers between high- and low-dose strategies.
- Additionally, the change in biomarkers from baseline to 72 or 96 h was not associated with differences in the outcomes of time to death or HF hospitalization.

Mentz RJ, et al. JACC Heart fail. 2015;3:97–107.

DAD-HF trial

- Recent studies suggest that transient WRF may not affect post-discharge outcomes.

- This theory is redemonstrated in both the Dopamine in Acute Decompensated Heart Failure (DAD-HF) and Renal Optimization Strategies Evaluation in Acute Heart Failure (ROSE-AHF) trials.

- In the DAD-HF trial, patients admitted for ADHF were randomized to receive either high-dose furosemide via continuous infusion (20 mg/h) or low-dose furosemide via continuous infusion (5 mg/h) along with low-dose dopamine (5 μg/kg/min).
- There were no differences in 60-day all-cause mortality or readmission rates despite a higher rate of worsening renal function at 24 h in the high-dose furosemide group (p=1 and p = 0.254, respectively)

Giamouzis G et al. Dopamine in Acute Decompensated Heart Failure (DAD-HF) Trial. J Card Fail. 2010;16:922–30

DAD-HF II trial

- The DAD-HF II trial investigated differences in all-cause mortality or heart failure hospitalizations between three separate groups:
  - high-dose furosemide (20 mg/h),
  - low-dose furosemide (5 mg/h) with lowdose dopamine (5 μg/kg/min),
  - low-dose furosemide alone.

- There was no significant difference between the groups with regards to all-cause mortality, heart failure rehospitalizations, or any additional benefit observed with the use of low-dose dopamine at day 60 ($p = 0.74$ and $p = 0.55$, respectively) or at 1 year of follow up ($p=0.84$ and $p = 0.40$, respectively).

Triposkiadis FK et al. the Dopamine in Acute Decompensated Heart Failure II (DAD-HF II) trial. Int J Cardiol. 2014;172:115–21

ROSE-AHF trial

- In the ROSE-AHF trial, the investigators explored the hypothesis that low-dose dopamine or low-dose nesiritide in addition to loop diuretic therapy would enhance decongestion while preserving renal function.
- Patients admitted with ADHF and renal dysfunction (GFR 15–60 mL/min/1.73 m^2) were randomized to receive low-dose dopamine or nesiritide, in addition to standard diuretic therapy, compared to a placebo group.
- There were no differences between the two groups when compared to placebo for the endpoints of enhanced diuresis or preservation of renal function at 72 h (cumulative urine volume for dopamine vs placebo p=0.59 and for nesiritide vs placebo p=0.49; change in cystatin C level for dopamine vs placebo p=0.72 and for nesiritide vs placebo p=0.36).

Chen HH et al. The ROSE acute heart failure randomized trial. JAMA. 2013;310:2533–43.

Other Approaches and Future Directions

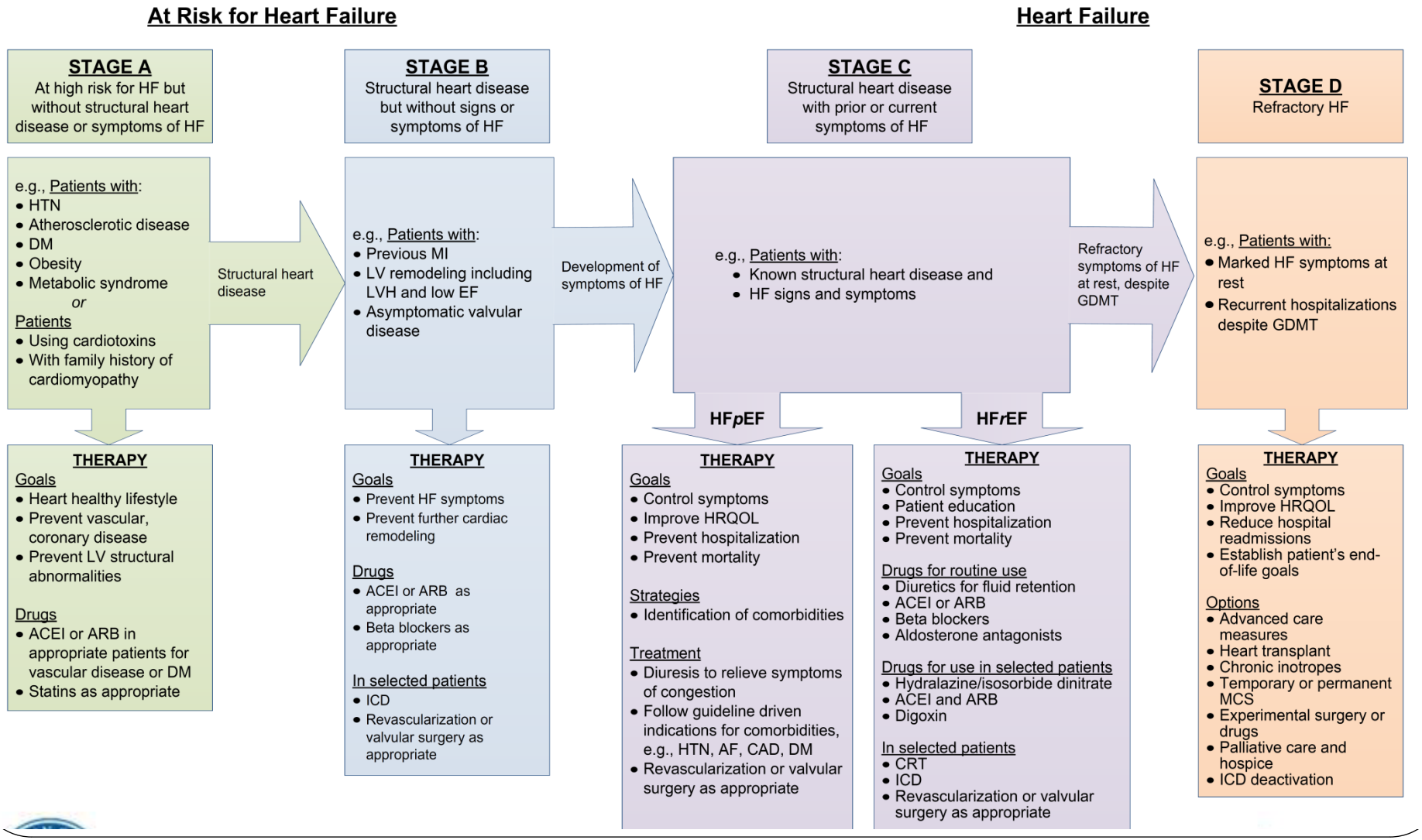
- The use of extracorporeal ultrafiltration is a theoretically attractive method with which to remove sodium chloride and water, with less stimulation of the renin–angiotensin–aldosterone system and a lower risk of rehospitalization than the risk associated with the use of diuretics
- A trial comparing ultrafiltration with a steppedcare pharmacologic approach in patients with heart failure and the cardiorenal syndrome showed similar fluid removal but more renal dysfunction and adverse events with ultrafiltration
- The combination of hypertonic saline with high doses of loop diuretics has been proposed to mitigate renal dysfunction and promote natriuresis, although that approach has not yet been tested in robust trials.
- Furosemide has been reformulated for subcutaneous delivery, which may allow delivery of “intravenous-like” diuretics outside the hospital setting, with potentially important implications for care delivery and cost. This approach is now being tested in a clinical trials.

Guidelines

2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

Developed in Collaboration With the American Academy of Family Physicians, American College of Chest Physicians, and International Society for Heart and Lung Transplantation

Stages, Phenotypes and Treatment of HF



Classification of Recommendations and Levels of Evidence

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

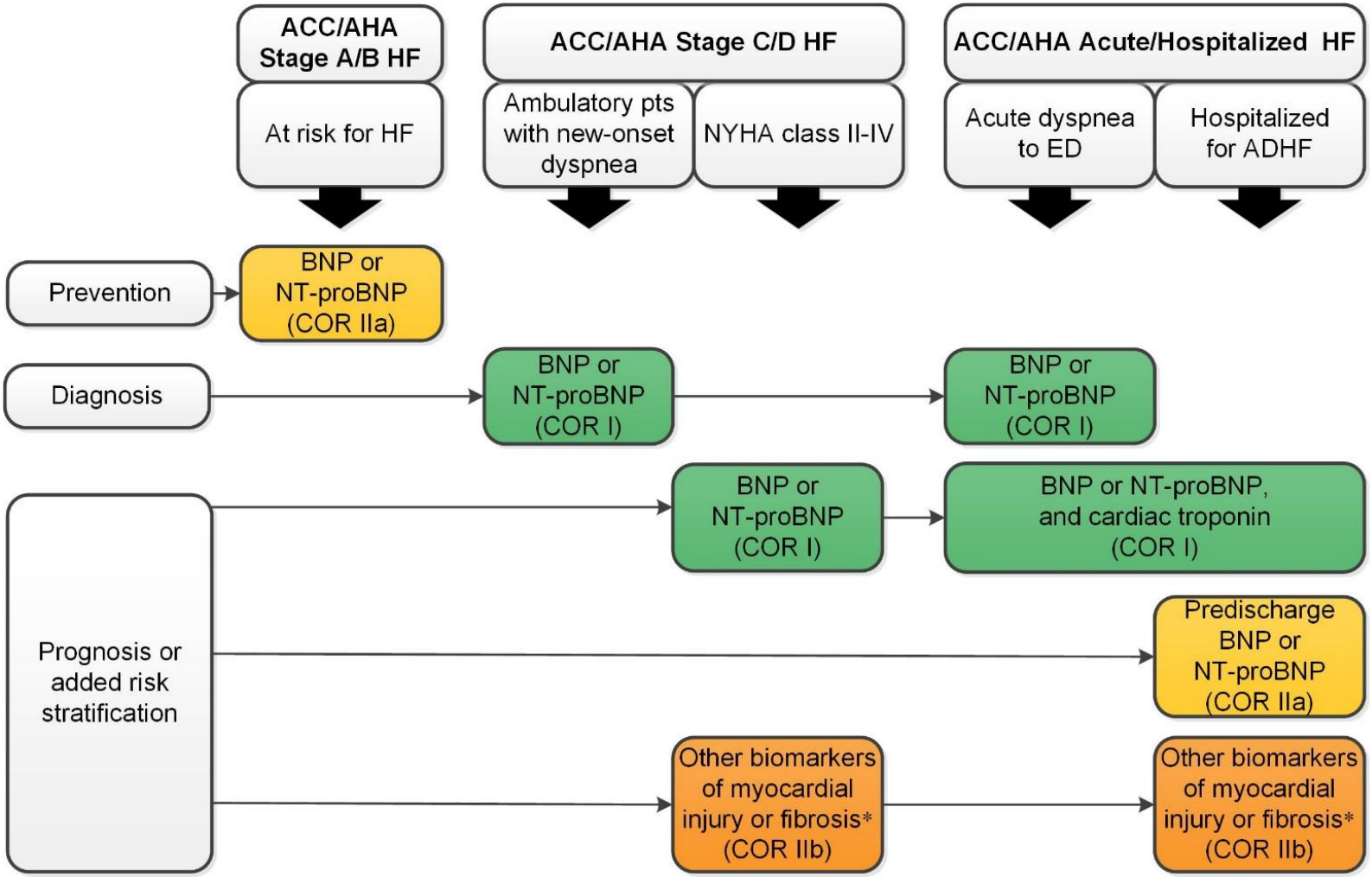
COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Initial and Serial Evaluation of Heart Failure

Initial and Serial Evaluation of Heart Failure

Biomarkers

Biomarkers Indications for Use



*Other biomarkers of injury or fibrosis include soluble ST2 receptor, galectin-3, and high-sensitivity troponin.
ACC indicates American College of Cardiology; AHA, American Heart Association; ADHF, acute decompensated heart failure; BNP, B-type natriuretic peptide; COR, Class of Recommendation; ED, emergency department; HF, heart failure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; and pts, patients.

Biomarkers

Biomarkers Indications for Use

COR	LOE	Recommendation	Comment/ Rationale
IIa	B-R	For patients at risk of developing HF, natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF.	NEW: New data suggest that natriuretic peptide biomarker screening and early intervention may prevent HF.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Biomarkers

Biomarkers for Diagnosis

COR	LOE	Recommendation	Comment/ Rationale
I	A	In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF.	MODIFIED: 2013 acute and chronic recommendations have been combined into a diagnosis section.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Biomarkers

Biomarkers for Prognosis or Added Risk Stratification

COR	LOE	Recommendations	Comment/ Rationale
I	A	Measurement of BNP or NT-proBNP is useful for establishing prognosis or disease severity in chronic HF.	2013 recommendation remains current.
I	A	Measurement of baseline levels of natriuretic peptide biomarkers and/or cardiac troponin on admission to the hospital is useful to establish a prognosis in acutely decompensated HF.	MODIFIED: Current recommendation emphasizes that it is admission levels of natriuretic peptide biomarkers that are useful.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Biomarkers

Biomarkers for Prognosis or Added Risk Stratification

COR	LOE	Recommendations	Comment/ Rationale
IIa	B-NR	During a hospitalization for HF, a predischarge natriuretic peptide level can be useful to establish a postdischarge prognosis.	NEW: Current recommendation reflects new observational studies.
IIb	B-NR	In patients with chronic HF, measurement of other clinically available tests, such as biomarkers of myocardial injury or fibrosis, may be considered for additive risk stratification.	MODIFIED: 2013 recommendations have been combined into prognosis section, resulting in LOE change from A to B-NR.

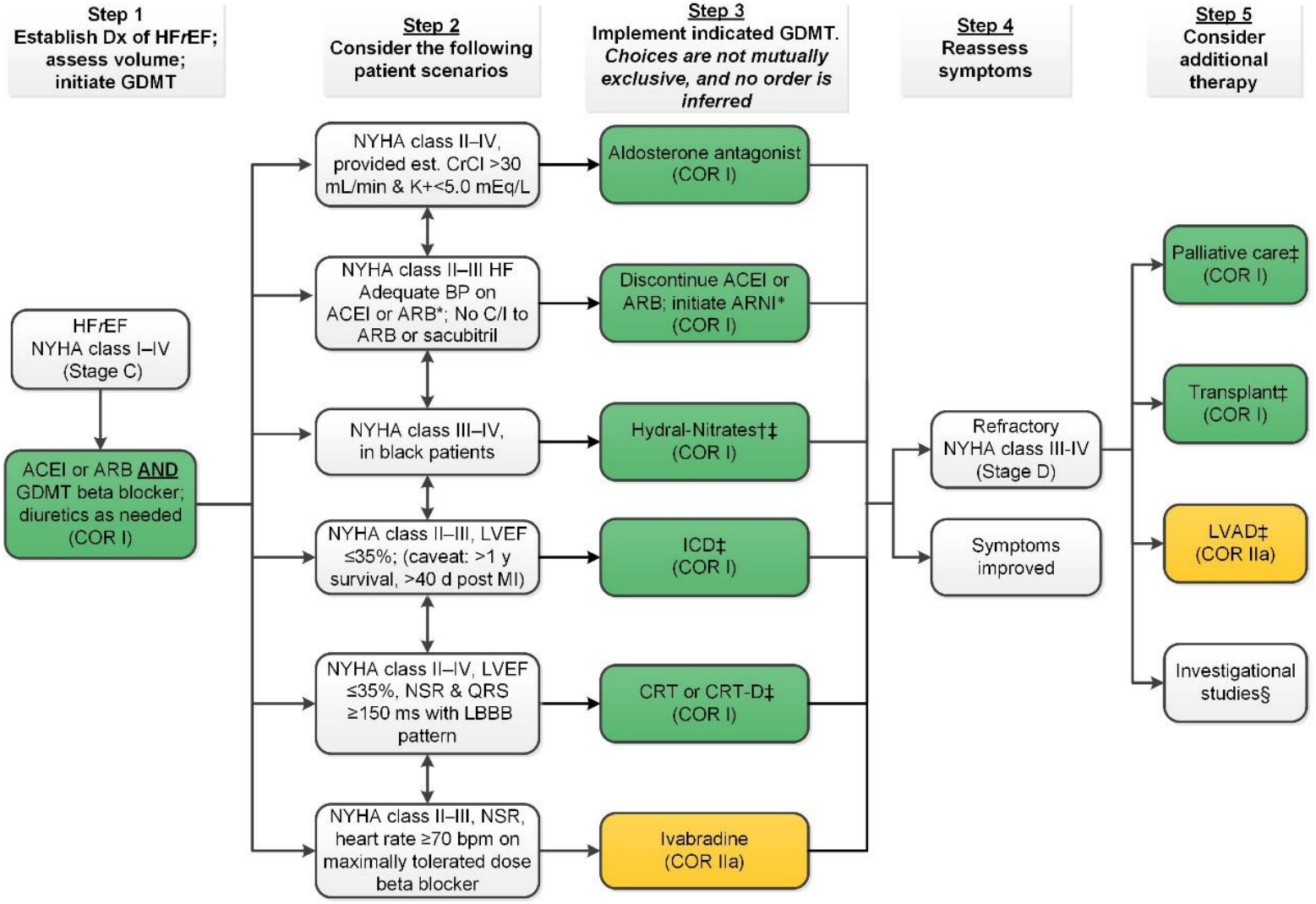
Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Treatment of HF Stages A Through D

Treatment of HF Stages A Through D

Stage C

Treatment of HFrEF Stage C and D



†Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored.
‡See 2013 HF guideline.
§Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF.

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy–device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; ISDN/HYD, isosorbide dinitrate hydral-nitrates; K+, potassium; LBBB, left bundle-branch block; LVAD, left ventricular assist device;

Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

COR	LOE	Recommendations	Comment/ Rationale
I	ACE-I: A	The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors (Level of Evidence: A), OR ARBs (Level of Evidence: A), OR ARNI (Level of Evidence: B-R) in conjunction with evidence-based beta blockers, and aldosterone antagonists in selected patients, is recommended for patients with chronic HF*r*EF to reduce morbidity and mortality.	NEW: New clinical trial data prompted clarification and important updates.
	ARB: A		
	ARNI: B-R		

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

COR	LOE	Recommendations	Comment/ Rationale
I	ACE-I: A	The use of ACE inhibitors is beneficial for patients with prior or current symptoms of chronic HF*r*EF to reduce morbidity and mortality.	2013 recommendation repeated for clarity in this section.
I	ARB: A	The use of ARBs to reduce morbidity and mortality is recommended in patients with prior or current symptoms of chronic HF*r*EF who are intolerant to ACE inhibitors because of cough or angioedema.	2013 recommendation repeated for clarity in this section.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

COR	LOE	Recommendations	Comment/ Rationale
I	ARNI: B-R	In patients with chronic symptomatic HF*r*EF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.	NEW: New clinical trial data necessitated this recommendation.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

COR	LOE	Recommendations	Comment/ Rationale
III: Harm	**B-R**	ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor.	NEW: Available evidence demonstrates a potential signal of harm for a concomitant use of ACE inhibitors and ARNI.
III: Harm	**C-EO**	ARNI should not be administered to patients with a history of angioedema.	NEW: New clinical trial data.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Pharmacological Treatment for Stage C HF With Reduced EF

Ivabradine

COR	LOE	Recommendations	Comment/ Rationale
IIa	**B-R**	Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF*r*EF (LVEF ≤35%) who are receiving GDEM*, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.	NEW: New clinical trial data.

*In other parts of the document, the term "GDMT" has been used to denote guideline-directed management and therapy. In this recommendation, however, the term "GDEM" has been used to denote this same concept in order to reflect the original wording of the recommendation that initially appeared in the "2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure".

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
I	B	Systolic and diastolic blood pressure should be controlled in patients with HF*p*EF in accordance with published clinical practice guidelines to prevent morbidity	2013 recommendation remains current.
I	C	Diuretics should be used for relief of symptoms due to volume overload in patients with HF*p*EF.	2013 recommendation remains current.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
IIa	**C**	Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HF*p*EF despite GDMT.	2013 recommendation remains current.
IIa	**C**	Management of AF according to published clinical practice guidelines in patients with HF*p*EF is reasonable to improve symptomatic HF.	2013 recommendation remains current.
IIa	**C**	The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HF*p*EF.	2013 recommendation remains current.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
IIb	B-R	In appropriately selected patients with HF*p*EF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate >30 mL/min, creatinine <2.5 mg/dL, potassium <5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations.	NEW: Current recommendation reflects new RCT data.
IIb	B	The use of ARBs might be considered to decrease hospitalizations for patients with HF*p*EF.	2013 recommendation remains current.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
III: No Benefit	**B-R**	Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HF*p*EF is ineffective.	NEW: Current recommendation reflects new data from RCTs.
III: No Benefit	**C**	Routine use of nutritional supplements is not recommended for patients with HF*p*EF.	2013 recommendation remains current.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Important Comorbidities in HF

Important Comorbidities in HF

Anemia

Anemia

COR	LOE	Recommendations	Comment/ Rationale
IIb	**B-R**	In patients with NYHA class II and III HF and iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation is <20%), intravenous iron replacement might be reasonable to improve functional status and QoL.	NEW: New evidence consistent with therapeutic benefit.
III: No Benefit	**B-R**	In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality.	NEW: Current recommendation reflects new evidence demonstrating absence of therapeutic benefit.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Important Comorbidities in HF

Hypertension
(New Section)

Hypertension

Treating Hypertension to Reduce the Incidence of HF

COR	LOE	Recommendations	Comment/ Rationale
I	B-R	In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg.	NEW: Recommendation reflects new RCT data.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Hypertension

Treating Hypertension in Stage C HF*r*EF

COR	LOE	Recommendations	Comment/ Rationale
I	C-EO	Patients with HF*r*EF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.	NEW: Recommendation has been adapted from recent clinical trial data but not specifically tested per se in a randomized trial of patients with HF.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Hypertension

Treating Hypertension in Stage C HF*p*EF

COR	LOE	Recommendations	Comment/ Rationale
I	C-LD	Patients with HF*p*EF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.	NEW: New target goal blood pressure based on updated interpretation of recent clinical trial data.

Important Comorbidities in HF

Sleep Disorders

(Moved from Section 7.3.1.4, Treatment of Sleep Disorders in the 2013 HF guideline)

Sleep Disorders

COR	LOE	Recommendations	Comment/ Rationale
IIa	**C-LD**	In patients with NYHA class II–IV HF and suspicion of sleep disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable.	NEW: Recommendation reflects clinical necessity to distinguish obstructive versus central sleep apnea.
IIb	**B-R**	In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness.	NEW: New data demonstrate the limited scope of benefit expected from CPAP for obstructive sleep apnea.
III: Harm	**B-R**	In patients with NYHA class II–IV HF*r*EF and central sleep apnea, adaptive servo-ventilation causes harm.	NEW: New data demonstrate a signal of harm when adaptive servo-ventilation is used for central sleep apnea.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

European Heart Journal (2016) **37**, 2129–2200
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

European Heart Journal (2016) **37**, 2129–2200
doi:10.1093/eurheartj/ehw128

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

WHY?
To relieve breathlessness and oedema in patients with symptoms and signs of congestion.
IN WHOM AND WHEN?
Indications: 1. Potentially all patients with symptoms and signs of congestion, irrespective of LVEF. 2. When used, should hould always be used in combination with an ACE-I (or ARB), a beta-blocker, and an MRA in patients with HFrEF (unless any of these drugs is not tolerated contra-indicated), until signs of congestion have been relieved. 3. Thaizde diuretics can be used in patients with preserved renal function and mild symptoms of congestion. However, the majority patients require loop diuretics (or combined with a thiazide diuretic and an MRA) due to the severity of HF symptoms and steadlily deterioriating kidney function.
Contra-indications: 1. Not indicated if the patient has never had symptoms or signs of congestion. 2. Known allergic reaction/other adverse reaction (drug-specific).
Cautions/seek specialist advice: 1. Significant hypokalaemia (K+ ≤3.5 mmol/L) – may be made worse by diuretic. 2. Significant renal dysfunction (creatinine >221 μmol/L [>2.5 mg/dL] or eGFR <30 mL/min/1.73 m^2) – may be made worse by diuretic or patient may not respond to diuretic (especially thiazide diuretic). 3. Symptomatic or severe asymptomatic hypotension (systolic blood pressure <90 mmHg) – may be made worse by diuretic-induced hypovolaemia. 4. Drug interactions to look out for: o Combination with ACE-I ARB or renin inhibitors[a] –risk of hypotension (usually not a problem). o Combination with other diuretics (e.g. loop plus thiazide)–risk of hypovolaemia, hypotension, hypokalaemia, and renal impairment.[b] o NSAIDs[c] – may attenuate effects of diuretic.

2016 ESC Guidelines. Ponikowski P et al. Eur J Heart Fail. 2016 Aug;18(8):891-975.

European Heart Journal (2016) **37**, 2129–2200
doi:10.1093/eurheartj/ehw128

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

WHICH DIURETIC AND WHAT DAILY DOSE? - see Table 7.3

Loop diuretics:
Furosemide: starting dose 20–40 mg, usual dose 40–240 mg
Bumetanide: starting dose 0.5–1.0 mg, usual dose 1–5 mg
Torasemide: starting dose 5–10 mg, usual dose 10–20 mg
Thiazides:
Bendroflumethiazide: starting dose 2.5, mg usual dose 2.5–10 mg
Hydrochlorothiazide: starting dose 25 mg, usual dose 12.5–100 mg
Metolazone: starting dose 2.5 mg, usual dose 2.5–10 mg
Non-thiazide sulfonamide:
Indapamide: starting dose 2.5 mg, usual dose 2.5–5 mg

WHERE?

In the community for most patients.

HOW TO USE?

- Check renal function and electrolytes.
- Start with a low dose (see Table 7.3), but an effective dose for a patient to achieving positive diuresis with a simultaneous reduction of body weight by 0.75–1,0 kg per day.
- Adjust dose according to symptoms and signs of congestion, blood pressure, and renal function. Use minimum dose necessary to maintain euvolaemia – the patient's 'dry weight' (i.e. to keep the patient free of symptoms and signs of congestion).
- Dose may need to be increased or decreased according to the patient's volume status (Remember that excessive diuresis is more dangerous than oedema itself).
- Re-check blood chemistry 1–2 weeks after initiation and after any increase in dose (urea/BUN, creatinine, K+).
- When to stop up-titration, reduce dose, stop treatment – see PROBLEM SOLVING.
- Patients can be educated to alter their own diuretic dose, according to need (based on symptoms, signs and weight changes – see Section 14).
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), biochemical monitoring, and dose adjustment (including patient educated in dose adjustment).

2016 ESC Guidelines. Ponikowski P et al. Eur J Heart Fail. 2016 Aug;18(8):891-975.

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2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

PROBLEM SOLVING

Asymptomatic low blood pressure:

- Dose may be reduced if no symptoms or signs of congestion.

Symptomatic hypotension:

- Causing dizziness/light headedness – reduce dose if no symptoms or signs of congestion.
- Reconsider need for nitrates, CCBs[d] and other vasodilators.
- If these measures do not solve problem, seek specialist advice.

Hypokalaemia/hypomagnaesaemia:

- Increase ACE-I/ARB dose.
- Add MRA, potassium supplements; magnesium supplements.

Hyponatraemia:

- Volume depleted:
  - Stop thiazide or switch to loop diuretic, if possible.
  - Reduce dose/stop loop diuretics if possible.
- Volume overloaded:
  - Fluid restriction.
  - Increase dose of loop diuretic.
  - Consider AVP antagonist (e.g. tolvaptan if available).
  - i.v. inotropic support.
  - Consider ultrafiltration.

2016 ESC Guidelines. Ponikowski P et al. Eur J Heart Fail. 2016 Aug;18(8):891-975.

European Heart Journal (2016) **37**, 2129–2200
doi:10.1093/eurheartj/ehw128

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

PROBLEM SOLVING (continued)

Hyperuricaemia/gout:
- Consider allopurinol prophylaxis.
- For symptomatic gout use colchicine for pain relief.
- Avoid NSAIDs.

Hypovolaemia/dehydration:
- Assess volume status; consider diuretic dosage reduction.

Insufficient diuretic response/diuretic resistance:
- Check adherence and fluid intake.
- Increase dose of diuretic.
- Consider switching from furosemide to bumetanide or torasemide.
- Add MRA/increase dose of MRA.
- Combine loop diuretic and thiazide/metolazone.[b]
- Administer loop diuretic twice (or more times) daily or on empty stomach.
- Consider short-term i.v. Infusion of loop diuretic.
- Consider ultrafiltration.

Renal impairment (rising creatinine/BUN–urea):
- Check for hypovolaemia/dehydration.
- Exclude use of other nephrotoxic agents, e.g. NSAIDs, trimethoprim.
- Withhold MRA.
- If using concomitant loop and thiazide diuretic stop thiazide diuretic.
- Consider reducing dose of ACE-I/ARB.
- Consider haemofiltration/dialysis.

ACC/AHA/HFSA FOCUSED UPDATE

CLINICAL STATEMENTS AND GUIDELINES

2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America

ACC/AHA/HFSA FOCUSED UPDATE

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CLINICAL STATEMENTS AND GUIDELINES

Diuretics in Hospitalized Patients

Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to reduce morbidity.

If patients are already receiving loop diuretic therapy, the initial intravenous dose should equal or exceed their chronic oral daily dose and should be given as either intermittent boluses or continuous infusion. Urine output and signs and symptoms of congestion should be serially assessed, and the diuretic dose should be adjusted accordingly to relieve symptoms, reduce volume excess, and avoid hypotension.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

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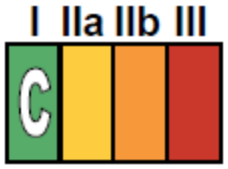
Diuretics in Hospitalized Patients (cont.)



The effect of HF treatment should be monitored with careful measurement of fluid intake and output, vital signs, body weight that is determined at the same time each day, and clinical signs and symptoms of systemic perfusion and congestion. Daily serum electrolytes, urea nitrogen, and creatinine concentrations should be measured during the use of intravenous diuretics or active titration of HF medications.

When diuresis is inadequate to relieve symptoms, it is reasonable to intensify the diuretic regimen using either:

a. higher doses of intravenous loop diuretics.
b. addition of a second (e.g., thiazide) diuretic.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

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Diuretics in Hospitalized Patients (cont.)

Low-dose dopamine infusion may be considered in addition to loop diuretic therapy to improve diuresis and better preserve renal function and renal blood flow.

Yancy CW, 2017 ACC/AHA/HFSA Focused Update for the Management of Heart Failure. Circulation. 2017 Aug 8;136(6):e137-e161

Summary

- The skillful use of diuretic therapy remains fundamental to the successful management of heart failure.

- An understanding of the physiological effects as well as the pharmacokinetic and pharmacodynamic properties of these drugs is key for safe and effective use

- Despite the long-standing clinical experience with loop diuretics, clinical trials are providing insights into more effective diuretic use, with the goal of improving the care of patients with heart failure.